

Interaction between Selenium and Inorganic Mercury

by Maths Berlin*

Data on mercury and selenium interaction in the mammalian body are reviewed. Experimental data from studies on rats show that selenium interacts with mercury metabolism and toxicity after exposure to mercuric mercury. Autopsy data from workers exposed to mercury vapor indicate an association between mercury and selenium retention in the central nervous system, suggesting the formation of a mercury-selenium complex. In animal experiments, mercuric mercury interferes with selenium metabolism and toxicity. Available data do not, at present, permit deduction as to whether additional selenium intake in man, exposed to mercury vapor or mercuric mercury, will have any effect, beneficial or adverse.

Introduction

Since Parizek and Ostadalova (1) reported that selenite dramatically decreased acute nephrotoxicity of mercuric mercury in rats, a number of studies on mercury-selenium interaction have been reported in the literature, and speculations have been made about the importance of this interaction for the evaluation of health hazards connected with mercury concentrations in food and in the work environment. The intention of this paper is to summarize the present state of knowledge about the interaction between selenium and inorganic mercury, and to underline some of the important deficiencies in our present knowledge. It is important for the reader to keep in mind that both selenium and mercury are metabolized differently in different species (2). The toxic effects, especially the dose-response relationships, of both elements differ also between different species. The toxic effects of selenium and mercury are also dependent on the chemical form presented to the organism.

This review will focus on the effects on man. Data from animal studies will be used for predicting effects on man or to elucidate the mechanisms involved.

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Metabolism and Toxicity

Selenium

Available data indicate that, in man, selenium compounds are metabolized into selenite, as in the rat, and transformed by methylation into trimethylselenonium ($(\text{CH}_3)_3\text{Se}^+$, which is excreted in urine (3). With excessive intake of selenium, dimethyl selenide, $(\text{CH}_3)_2\text{Se}$, is formed and exhaled. Dose-response relationships or levels for toxic effects of selenium in critical organs are not well-known and seem to vary between different species (4). With excessive intake of selenium, the liver and the central nervous system are affected in animals. Man seems to be less sensitive to excessive selenium intake, although a few cases of intoxication have been described (3). The daily intake of selenium in the American diet is about 150 μg (5), which corresponds to an average of about 0.005 ppm selenium in food.

Inorganic Mercury

Exposure to inorganic mercury occurs with two forms of inorganic mercury: mercuric salts and elemental mercury or mercury vapor. For mercuric salts, the critical organ in mammals and man is the kidney; for mercury vapor, the critical organ is the

brain. In both types of exposure, the elimination is mainly via feces and urine and is dose-dependent. There is more elimination by urine at higher doses; a small fraction is exhaled. Mercury vapor is taken up by the blood, and physically dissolved vapor can probably be transported and transmitted into the brain, where it is oxidized to mercuric mercury. Mercuric mercury taken up in the blood is partly bound to plasma proteins and to blood cells, transported into the tissue, and to a large extent accumulated in the kidney.

Little is known about the interspecies differences in plasma protein binding of mercuric mercury. However, data on distribution in blood and between organs indicate considerable species differences (6). Also, as to transport of elemental mercury in blood to the brain, few data are available about the mechanism and the possible differences between species in this respect. Concentrations in the critical organs—the brain and the kidney—associated with toxic manifestations in mammals are around 10 $\mu\text{g/g}$ (7). The daily intake of mercury is about 2.89 μg for man (5). Probably a large part of this is in the form of methylmercury.

Selenium Interaction with Mercuric Mercury Toxicity

Several authors (1, 8–11) have demonstrated that if selenium is given in equimolar doses together with mercuric mercury, this has, in the rat, a protective effect against nephrotoxicity. Selenium administration is combined with a changed distribution of mercury, with increasing amounts in blood and in liver, and an increase in total body retention of mercury. Selenium also causes an increase in kidney retention of mercury, although toxic manifestation is absent (10). Mercury and selenium have been demonstrated in inclusion bodies in both reticular endothelial cells and kidney tubular cells (10). No data on selenium interaction on mercuric mercury toxicity in man are available.

Selenium Interaction with Elemental Mercury Toxicity and Metabolism

No animal data are available concerning interaction between selenium and neurotoxicity of elemental mercury. However, studies on workers and populations exposed to mercury vapor indicate a remarkable correlation between selenium and mercury retention in brain, thyroid, and hypophysis with mercury–selenium concentration close to 1:1 molar ratio. Thus, Kosta et al. (12) report mercury levels of up to 13 ppm in brain of mercury-exposed workers with no obvious clinical signs of intoxica-

tion. A value of 13 ppm was found in a man exposed for 33 years, followed by 16 years (retirement) without exposure. Remarkably high levels of mercury in brain from persons with high levels of exposure in early life followed by a long time of no exposure and no obvious neurological signs have been reported by several authors (13, 14). The close correlation between mercury and selenium content in the brain found by two authors (12, 15), and the remarkably long retention time of mercury in the brain indicate an association between selenium and mercury storage in the human central nervous system.

Mercury Interaction with Selenium Toxicity and Metabolism

Parizek et al. (8, 9) have demonstrated that mercury interacts with selenium metabolism and toxicity in rats. This effect was obtained with a toxic dose of mercuric acetate (5 $\mu\text{mo k/kg}$ body weight). Given before administration of selenium in equimolar doses, mercury inhibited exhalation of dimethyl selenide. Given after administration of the selenium compound, mercury enhanced the toxic effect of dimethyl selenide formed or injected. Mercury and selenium reciprocally inhibited passage of selenium and mercury to the fetus and increased the retention of each other in the mother. Data on mercury interference with selenium metabolism in man is lacking.

Summary and Concluding Remarks

From available data it is obvious that mercury and selenium interact in the mammalian body, and a formation of a selenium–mercury complex is likely, at least temporarily, although such a complex has not as yet been identified chemically in biological material. Data are not yet available about dose–response relationships for mercury–selenium interaction in man. It is thus not possible at present to deduce whether additional selenium intake in man exposed to mercury vapor or mercuric mercury will have any effect, beneficial or adverse, or what dose of mercuric mercury or mercury vapor which may produce a selenium deficiency or enhance selenium toxicity in man. Most data so far available are derived from studies in rats at rather unrealistic dose levels. However, it can be pointed out that selenium–mercury interaction offers an explanation for the remarkably long retention and accumulation of mercury in brain, without obvious neurological effects, reported by several authors.

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